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Investigating the association between hyperprolactinemia and thyroid autoimmunity in women

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ABSTRACT

Aims: Hyperprolactinemia (HPRL), a condition characterized by elevated levels of prolactin (PRL) hormone, is considered to be related to various autoimmune diseases, such as thyroid autoimmunity (TAI). The association between HPRL and TAI still evokes controversy. Our study intends to examine the possible relationship between HPRL and TAI in young women.

Methods: This retrospective study was done between January 2018 and December 2022, including 90 women with HPRL and 90 control subjects of similar age and gender. A retrospective examination was conducted on the medical records of 90 patients with HPRL to gather relevant data. Information regarding related parameters was analyzed and compared to the control group data.

Results: Our results found that thyroid stimulating hormone (TSH) levels were notably elevated in patients with HPRL compared to healthy women (2.24 vs. 1.86). Also, a statistically significant association between the case and control regarding serum free triiodothyronine (fT3) ($p<0.05$). No statistically significant difference was found between the case and control regarding serum free thyroxin (fT4) ($p>0.05$). Patients with HPRL demonstrated considerably higher anti thyroperoxidase antibody (anti-TPO) levels (46.08 vs. 43.95). Significantly elevated antithyroglobulin antibody (anti-Tg) levels were observed in patients with HPRL (1.07 vs. 0.84).

Conclusion: The study suggests a potential link between HPRL and TAI. Further research is needed to explore this relationship and its implications for patient care.

Keywords: Hyperprolactinemia, HPRL, thyroid autoimmunity, autoimmune diseases

INTRODUCTION

Hyperprolactinemia (HPRL), a condition characterized by elevated levels of prolactin (PRL) hormone, has been associated with various autoimmune diseases, such as thyroid autoimmunity (TAI).[1] TAI, on the other hand, is the most frequent autoimmune disease among reproductive-aged women and is associated with conditions such as Hashimoto's thyroiditis and Graves' disease. Autoimmune thyroid diseases affect a significant portion of the population and it can be also associated with low β-HCG levels in pregnant women and iron deficiency anemia.[2,3] Research has shown that 20% of autoimmune thyroid disease patients have HPRL, with twice the occurrence in those with hypothyroidism.[4]

Moreover, studies have reported that thyroid autoantibodies are seen in 25% of patients with HPRL than in 22% of controls.[5] Although HPRL and TAI have been widely studied, the relationship between these conditions remains unclear and warrants further investigation.

Some studies have found no increased prevalence of TAI among individuals diagnosed with HPRL in comparison to healthy controls.[6] However, other research has shown that patients with HPRL have a notable increase in the volume of thyroid, the prevalence of thyroid nodules, and autoimmunity among the population studied.[7] Additionally, another study shows that female patients with prolactinomas are more likely to have autoimmune thyroid diseases than the general population.[8] The prevalence of clinical symptoms, such as dry skin and cold weather intolerance, is not reported in patients with HPRL, with a significant difference compared to those without it.[9]

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The main contribution of this study is to investigate the possible relationship between HPRL and TAI in young Turkish women. The association between autoimmune thyroid disease activity and PRL levels remains controversial. Our study aims to examine the possible relationship between HPRL and TAI. By identifying any potential association between HPRL and TAI, our study may add to a more in-depth understanding of the pathogenesis of these conditions and inform the development of new treatment options.

METHODS

This retrospective study was conducted on patients between January 2018 and December 2022. The study was approved by Bezmialem Vakıf University Hospital Ethics Committee (Date: 03/04/2023, Decision No: 2023/74). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

By concentrating on patients with autoimmune features, this study intends to investigate the link between HPRL and primary thyroid diseases. The study's sample size was 90 women with HPRL and 90 age and gender-matched control subjects. A retrospective examination of the medical records of the study subjects was conducted to gather relevant data. Information regarding thyroid-stimulating hormone (TSH), free triiodothyronine (fT3), circulating free thyroxine (fT4), anti thyroperoxidase (anti-TPO), and antithyroglobulin (anti-Tg) was analyzed.

The study did not include women using medications affecting thyroid and prolactin levels. Women who had chronic diseases and were not between 25-40 years old were also excluded from the study.

In order to assess TAI, the study compared the frequency of elevated anti-Tg and/or anti-TPO levels among patients and control subjects. The link between serum PRL levels and thyroid autoantibodies was also examined. Finally, the study analyzed the relationship between HPRL and TAI. Following this methodological approach, the study aimed to provide valuable insights into the potential connection between thyroid disorders and HPRL, emphasizing patients with autoimmune traits.

Statistical Analysis

The study used medians (range) to report the data results. To compare the data between groups, the Mann-Whitney U test was employed, which is appropriate for non-normal distributions. SPSS software (version 18.0, SSPS Inc., Chicago, IL, USA) was used to perform the statistical analysis. The threshold for statistical significance was set at a p-value of less than 0.05.

RESULTS

This study included one hundred eighty age-matched (31.77±3.94) and body mass index (BMI) matched (24.98±0.99) women. Table 1 shows descriptive statistics of the parameters of the study in women.

Table 1. Statistical description of study parameters in participants

Study parameters	median (range) mean ± SD
Age	33 (24-39) 31.77 ± 3.94
BMI	24 (22-28) 24.98±0.99
TSH	2 (1.48-2.96) 2.12 ± 0.42
fT3	3 (2.74-1.47) 2.98 ± 0.18
fT4	1 (0.88-1.52) 1.14 ± 0.21
Anti-TPO	10 (3-66) 28.87 ± 19.74
Anti-Tg	2 (1.45-6) 19.69 ± 18.15

BMI:Body mass index; TSH: thyroid stimulating hormone; fT3: free triiodothyronin ; fT4: free thyroxine; anti-TPO: anti thyroperoxidase antibody; anti-Tg: antithyroglobulin antibody.

Two groups were formed for the study: Group 1, which had 90 patients (mean age: 31.44 ± 2.19), and Group 2, comprising 90 control subjects (mean age: 31.98 ± 2.89). The mean BMI of group 1 was (25.06 ± 1.01) and group 2 was (24.77 ± 0.96). There were no notable differences in age between the two groups ($p > 0.05$).

Table 2. Comparison of case and control groups

Study parameters	Case (patients with hyperprolactinemia)	Control (n=90) M±SD	p-value
(n=90) M±SD	Control	31.98±2.89	0.879
(n=90) M±SD	p-value	24.77±0.96	0.749
Age	31.44±2.19	31.98±2.89	0.879
BMI	25.06±1.01	24.77±0.96	0.749
TSH	2.24±1.36	1.86±1.19	<0.001
fT3	3.35±1.59	3.01±1.3	0.028
fT4	1.28±0.68	1.18±0.61	0.09
Anti-TPO	46.08±5.86	43.95±2.27	0.034
Anti-Tg	1.07±0.28	0.84±0.51	<0.001

As stated in Table 2, a statistically significant association was observed between the case and control regarding serum TSH ($p<0.05$). Patients with HPRL had significantly higher TSH levels than healthy controls (2.24 vs. 1.86).

As stated in the table above, a statistically significant association was observed between the case and control regarding fT3 ($p<0.05$). The fT3 levels were significantly higher in patients with HPRL (3.35 vs. 3.01). The case and control groups did not demonstrate a statistically significant difference regarding fT4 ($p>0.05$).

As stated in the table above, a Mann-Whitney U test found a statistically significant association between case and control regarding Anti-TPO ($p<0.05$). Anti-TPO levels were significantly higher in patients with HPRL (46.08 vs. 43.95).

Table 2 showed a statistically significant association between case and control regarding Anti-Tg ($p<0.05$). Anti-Tg levels were significantly higher in patients with HPRL (1.07 vs. 0.84). Figure shows the study's findings and parameters' differences in the groups.

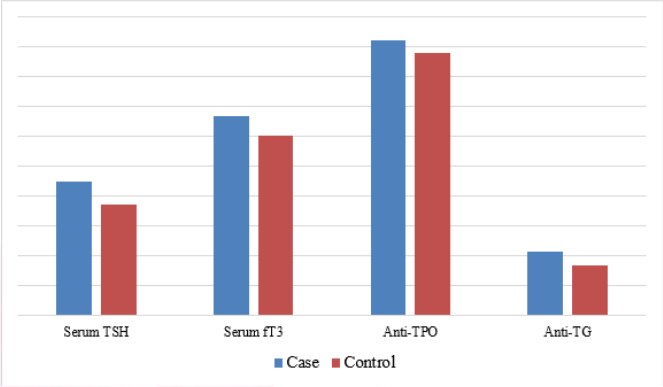

Figure. Study's findings and parameters' differences in the groups

DISCUSSION

This study investigated the possible relationship between HPRL and TAI. It is important to study the relationship between TAI and HPRL because high prolactin may have caused hypothyroidism or vice versa. Reduction of thyroid in the body can cause prolactin to increase or decrease. As a result, if a woman has hypothyroidism and her prolactin is high, prolactin treatment can return the thyroid to normal. Therefore, identifying the influential factors can provide more effective treatments.

The findings indicated that compared to healthy controls, TSH, fT3, anti-TPO, and anti-Tg levels were significantly elevated in patients with HPRL. The current findings are in agreement with previous studies that have reported a relationship between HPRL and thyroid dysfunction. For instance, a study by Sahu et al.[10] found significantly increased serum PRL levels in patients with both clinical and subclinical hypothyroidism, and HPRL was observed in 22.9% of patients with subclinical hypothyroidism and 8.3% of clinical hypothyroidism. In another study conducted by Kumari et al.[11] a positive association between PRL levels and serum TSH was observed in infertile women. The study identified HPRL in 7% of the control group and 57% of infertile women.

Other studies have also reported the association between HPRL and TAI. A study by Unluturk et al.[11] found that among patients exhibiting autoantibody positivity, thyroid function test irregularities were more prevalent in HPRL patients (60%) compared to controls (9.1%). Similarly, Sahu et al.[9] conducted a study that found a correlation between PRL and TSH levels in patients with clinical and subclinical hypothyroidism.

While several studies have reported a relationship between HPRL and TAI, some studies have not found a significant association between the two conditions. For example, in a study by Onal et al.[12] untreated prolactinoma patients did not exhibit an increased incidence of TAI when compared to healthy individuals. Similarly, a study by Venables et al.[13] showed that TAI does not influence the outcomes of the pregnancy in either euthyroid women or women with subclinical hypothyroidism.

One study examined a total of 100 patients diagnosed with HPRL and found that 25% of them had positive anti-TPO and anti-Tg, which are markers of TAI. Among these patients, the frequency of thyroid function test abnormalities was higher than in controls.[11] Another study found that patients with HPRL had a higher prevalence of TAI than controls, but the difference was not statistically significant.[14]

Other research has examined the impact of iodine supplementation on TAI and found that while iodine prophylaxis may have some risks for TAI, in a population with a stable median iodine concentration of up to 300 µg/L, the benefits are significantly greater than the risks.[15] The pathogenesis of TAI is complex and involves genetic and environmental factors. Environmental factors such as exposure to pollutants and endocrine disruptors have been implicated in developing autoimmune thyroid disease.[16]

The inconsistent results across studies could be attributed to several factors, such as differences in study populations, sample sizes, and methodologies. Additionally, the relationship between HPRL and TAI might be influenced by various factors that could act as confounders, such as gender, age, and comorbid autoimmune diseases.[17] It is also possible that the association between HPRL and TAI is not direct but mediated by other factors, such as hormonal imbalances or immune system dysregulation.[18]

The underlying mechanisms linking HPRL and TAI are not yet fully understood. However, it has been suggested that PRL levels may have immunomodulatory effects, influencing the immune response and contributing to the development of autoimmune thyroid diseases.[19] Additionally, thyroid-releasing hormone (TRH) stimulates the secretion of both PRL and TSH, which may lead to elevated PRL levels in patients with thyroid dysfunction.[20]

The relationship between HPRL and TAI is not fully understood, but several potential mechanisms have been proposed. One possible mechanism is that HPRL may trigger an autoimmune response that leads to TAI. PRL levels has been shown to have an immunostimulatory effect, mainly through the inhibition of autoreactive B lymphocytes' negative selection.[21] This effect may lead to the production of autoantibodies that attack the thyroid gland, causing TAI.[22] Another possible mechanism is that there may be a genetic link between HPRL and TAI. Chromosome 6's short arm contains the PRL gene, which is also associated with several autoimmune diseases, including autoimmune thyroiditis.[23] A third possible mechanism is that HPRL may affect the levels of thyroid hormones in the body, leading to TAI. PRL levels has been shown to inhibit the secretion of TSH, resulting in an effect on the synthesis of thyroid hormones by the thyroid gland.[24] Finally, it has been suggested that treating HPRL may lead to the development of TAI. Some medications used to treat HPRL, such as dopamine agonists, have been associated with developing autoimmune thyroiditis.[25]

In conclusion, the association between HPRL and TAI is complicated and not fully understood. Several potential mechanisms have been proposed, including autoimmune, genetic, hormonal, and treatment-related mechanisms. Further research is needed to fully understand the relationship between these two conditions.

Limitations of the Study

As with any study, our study also had some limitations. The first limitation is the cross-sectional design of the study, meaning it only provides a snapshot of the relationship between HPRL and TAI at a single point in time. This limits the ability to conclude causality or the direction of the relationship. The sample size is relatively small, with only 90 women with HPRL and 90 control subjects. Therefore, the findings may not be generalizable to other populations. This study did not include men because of the limited work done on Turkish women. The focus of the study was on women. Finally, the research was based on a retrospective examination of medical records to gather data, which may introduce bias or errors in the data collection. Despite these limitations, the study provides valuable insights into the potential association between HPRL and TAI, and further research is necessary to verify and expand upon our findings.

CONCLUSION

The current study explored the potential association between HPRL and TAI. Patients with HPRL exhibited significantly elevated levels of TSH, fT3, anti-TPO, and anti-Tg compared to healthy controls, according to the results. Previous research has reported a relationship between thyroid dysfunction and HPRL, which is consistent with the current findings. This study implies that patients presenting with HPRL or TAI should be evaluated for both conditions, as they may be closely related. More research is needed to elucidate the mechanisms and explore potential therapeutic approaches for patients with HPRL and TAI. Overall, this research contributes to the growing body of research on the correlations between HPRL and TAI, highlighting the importance of considering both conditions in clinical practice.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Bezmialem Vakıf University Hospital Ethics Committee (Date: 03/04/2023, Decision no: 2023/74).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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